DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

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APR 1 2005

Jerussi Consulting, Inc.
Attention: Robert A. Jerussi, Ph.D.
3311 Midland Road
Fairfax, VA 22031

Docket No. 2003P-0279/CP1

Dear Dr. Jerussi:

This is in response to your petition filed on June 18, 2003, requesting permission to file an Abbreviated New Drug Application (ANDA) for the following drug product: Fluocinolone Acetonide, 0.01%; Hydroquinone, 4%; and Tretinoin, 0.05% Topical Solution. The listed drug product to which you refer in your petition is Tri-Luma® (Fluocinolone Acetonide, 0.01%; Hydroquinone, 4%; and Tretinoin, 0.05%) Cream, NDA 21-112, held by Hill Dermaceuticals. We also reference our letter dated February 3, 2004, your amendment dated February 19, 2004, the comments submitted by Gray Cary on behalf of Hill Dermaceuticals, Inc. dated September 30, 2003, and your response to the comments dated February 5, 2004.

Your request involves a change in dosage form from that of the listed drug product (i.e., from cream to topical solution). The change that you request is the type of change that is authorized under Section 505(j)(2)(C) of the Act.

This petition was reviewed pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act). Under Sections 505(j)(2)(C)(i) of the Act such a petition will be approved unless the Food and Drug Administration (FDA) finds that investigations must be conducted to show the safety and effectiveness of the proposed drug product, or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug product.

The FDA has determined that your proposed change in dosage form raises questions of safety and effectiveness, and has concluded that clinical trials are required for this specific drug product.

In general, topical drugs have different drug delivery rates, deployability (look and feel), safety and efficacy depending on the vehicle in which they are contained. Bridging studies are needed to demonstrate the safety and effectiveness for a change from a cream formulation to a topical solution formulation. For topical preparations for the skin, as per 21 CFR 320.24(b)(4), well-controlled clinical trials that establish the safety and effectiveness of the drug product, for

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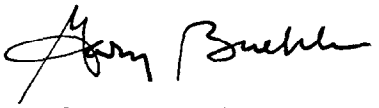
purposes of measuring bioavailability, or appropriately designed comparative clinical trials, for purposes of demonstrating bioequivalence are recommended. Please note that due to the fact that Tri-Luma® is a combination drug product, clinical studies to demonstrate safety and effectiveness may be more complex. A head to head placebo controlled clinical trial is necessary to establish efficacy for the proposed product. In addition, safety studies including but not limited to dermal safety studies, HPA axis suppression and the measurement of systemic absorption of hydroquinone and tretinoin are necessary factors to establish the safety of the proposed product. Therefore, FDA is denying the petition under Section 505(j)(2)(C)(i) because investigations are necessary to show the safety and effectiveness of the proposed drug product.

This petition is being denied because clinical trials are required for the approval of the requested change to the drug product. Therefore, the question of whether pediatric studies are necessary under the Pediatric Research Equity Act (PREA) has not been evaluated. Please contact the Division of Dermatologic and Dental Drug Products at (301) 827-2020 if you wish to pursue approval of your product under Section 505(b) of the Act.

If you disagree with our determination concerning the acceptability of your petition as originally submitted, you may seek a reconsideration of the denial following the procedures set forth in 21 CFR 10.33. Requests for reconsideration must be based solely on the information contained in your original petition and must be submitted in accordance with 21 CFR Section 10.20, in the format outlined in Section 10.33 and no later than 30 days after the date of the decision involved. Petitions for reconsideration should be filed with the Dockets Management Branch at the address listed below. If there is additional information, not included as part of your original submission that you would like the FDA to consider, you should submit a new petition including all the necessary information to the Dockets Management Branch.

A copy of this letter denying your petition will be placed on public display in the Dockets Management Branch, Room 1061, Mail Stop HFA-305, 5630 Fishers Lane, Rockville, MD 20852.

Sincerely yours,



Gary J. Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research